REMARKS

Reconsideration of the Office Action mailed February 26, 2003, (hereinafter "instant Office Action"), entry of the foregoing amendments and withdrawal of the rejection of claims 1-88, are respectfully requested.

In the instant Office Action, claims 1-88 are listed as pending, and claims 1-88 are listed as rejected.

Attached hereto as Appendix A is a marked-up version of the changes made to the claims by the current amendments. Appendix A is captioned **"Version with markings to show changes made"**.

The Examiner has rejected claims 1-88 under 35 U.S.C.§112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection. Applicants' response to the Examiner's enumerated points are numbered accordingly to track the Examiner's points.

i) With respect to the term "prodrug", Applicants maintain the arguments presented in the two Replies filed August 26, 2002 and November 26, 2002. Without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have deleted the term "prodrug" from claims 1, 33, 35, 37, 38, 40, 45, 46, and 48 without waiver or prejudice.

ii) With respect to the term "substituted", Applicants maintain the arguments presented in the two Replies filed August 26, 2002 and November 26, 2002. The Examiner asks how one can say for sure whether a given substituent is contemplated by Applicants or not. The test for definiteness under 35 U.S.C. §112, second paragraph, is whether "those skilled in the art would understand what is claimed when read in light of the specification". Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). A clear example of the extent of reliance on the knowledge of those skilled in the art is give in Orthokinetics (supra):

> It is undisputed that the claims require that one desiring to build and use a travel chair must measure the space between the selected automobile's doorframe and its seat and then dimension the front legs of the travel chair so they will fit in that particular space in that particular automobile. Orthokinetics' witnesses, who were skilled in the art, testified that such a task is evident from the specification and that

> one of ordinary skill in the art would easily have been able to determine the appropriate dimensions.
>
> The claims were intended to cover the use of the invention with various types of automobiles. That a particular chair on which the claims read may fit within some automobiles and not others is of no moment. The phrase "so dimensioned" is as accurate as the subject matter permits, automobiles being of various sizes. See Rosemount, Inc. v. Beckman Instruments, 727 F.2d 15400, 1547, 221 USPQ (BNA) 1, 7 (Fed. Cir. 1984). As long as those of ordinary skill in the art realized that the dimensions could be easily obtained, 35 U.S.C.§ 112, second paragraph, requires nothing more. The patent law does not require that all possible lengths corresponding to the spaces in hundreds of different automobiles be listed in the patent, let alone that they be listed in the claims.

The question of the dimensions of the travel chair in Orthokinetics is analogous to the question of which substituents can be used in the instant application. That is, the foregoing case provides support to Applicants' position that the patent law does not require that all possible substituents be listed for a compound. One of ordinary skill in the art would realize that suitable substituents could be determined by referencing the examples provided and utilizing the assays contained in the instant specification to determine whether the substituted compound in question would fall within Applicants' claims.

Further, the term "substituted" is a well-known term which is understood by one of ordinary skill in the art. Furthermore, Applicants have provided the description for routine assays to determine the activity of a compound as well as listing preferred compounds and preferred examples. Thus, as long as a substitution as taught and enabled by the instant application in view of the art results in a compound that is chemically stable and shows the desired activity, such a compound would fall within Applicants' definition of "substituted".

The Examiner also states that Applicants have not said whether dimers of the instant compounds, sugars, antibodies, nucleotides, are all intended or not. As stated in M.P.E.P. 2173.04, "Breadth of a claim is not to be equated with indefiniteness." In re Miller, 441 F.2d 689, 169, USPQ 597 (CCPA 1971). Furthermore, In re Borkowski, 57 CCPA 946; 422 F.2d 904; 1970 CCPA declares "If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph."

iv) Regarding the term "heterocyclic", Applicants maintain the arguments presented in the last two Replies filed August 26, 2002 and November 26, 2002. According to M.P.E.P.

2173.02, definiteness of claim language must be analyzed, not in a vacuum, but in light of a) the content of the particular application disclosure b) the teachings of the prior art and c) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Applicants have defined "heterocyclic" as including "heteroaryl", which is exemplified on page 53, line 24 to page 54, line 7 and "heterocycloalkyl", which is specifically defined on page 54, lines 17-20 of the instant specification. As the Examiner has acknowledged, Applicants have provided examples of heterocyclic compounds. Applicants have also listed preferred examples of compounds of the invention which include heterocyclic compounds and assays to be used in determining whether a heterocyclic compound falls within Applicants' claims. The meaning of the term "heterocyclic" is clear to one of ordinary skill in the art in light of reading the instant specification, reviewing its examples and assays, and referencing prior teachings.

v) The Examiner alleges that in claims 33 and 34 it is unclear why one would need to inhibit one or more protein kinase activity and that it is unclear who needs such inhibition and what is accomplished. Applicants respectfully direct the Examiner's attention to page 55, line 25 to page 56 line 20 wherein Applicants state "The compounds of this invention have antiangiogenic properties. These antiangiogenic properties are due at least in part to the inhibition of protein kinases essential for angiogenic processes." On page 55, line 27 to page 56, line 23 the specification lists diseases in which compounds of the invention can be used. On page 57, line 9-11 of the instant specification, Applicants describe that it is envisaged that the disorders listed are mediated to a significant extent by protein kinase activity of one or more protein kinases. Thus, inhibition of protein kinase activity would benefit one suffering from , at least, any of the diseases enumerated on page 55, line 27 to page 56, line 23.

Based upon the foregoing, the rejections of claims 1-88 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

The Examiner has rejected claims 33-51 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification to enable one to make or use the invention. Applicants respectfully traverse this rejection. Applicants' response to the Examiner's enumerated points are numbered accordingly to track the Examiner's points.

ii) Regarding the term "cancer", without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and

to place it in condition for allowance, Applicants have cancelled claim 41 without waiver or prejudice. Applicants have also cancelled claim 43 and incorporated its subject matter into claim 40.

iii) Regarding the term "affecting hyperproliferative disorders", without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have deleted the term "hyperproliferative disorders" from claim 35 without waiver or prejudice. Applicants have further amended claim 35 to add "thyroid hyperplasia, Grave's disease, cyst, hypervascularity of ovarian stroma characteristic of polycystic ovarian syndrome and polycystic kidney disease". Support for this amendment can be found, *inter alia*, at page 56, lines 7-9 of the instant specification.

iv) Regarding the term "affecting angiogenesis", Applicants respectfully direct the Examiner's attention to page 57, lines 11-19, wherein Applicants state, in part, "By inhibiting activity of these tyrosine kinases, the progression of the listed disorders is inhibited because the angiogenic...component is severely curtailed...certain compounds are inhibitors of FGFR, PDGFR, c-Met and IGF-1-R. These receptor kinases can directly or indirectly potentiate angiogenic...responses." Applicants further direct the Examiner's attention to page 55, line 25 wherein Applicants state "The compounds of this invention have antiangiogenic properties." Thus, the compounds of the instant invention affect angiogenesis.

v) Regarding the term "cardiovascular condition", without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have amended claim 40 to delete the term "cardiovascular condition" and cancelled claim 42 without waiver or prejudice. The subject matter of claim 42 has been incorporated into claim 40.

vi) Regarding the term "ocular condition", without conceding to the correctness of the Examiner's rejections and for the sole purpose of expediting prosecution of the instant application and to place it in condition for allowance, Applicants have deleted the term "ocular condition" from claim 40 and cancelled claim 41 without waiver or prejudice. The subject matter of claim 41 has been incorporated into claim 40.

Based upon the foregoing, the rejection of claims 33-51 under 35 U.S.C. §112, first paragraph, is obviated and should be withdrawn.

The Examiner has rejected claims 1-88 under 35 U.S.C. §103(a) as allegedly being unpatentable over Altmann et al. (WO 97/49706). Applicants respectfully traverse this rejection. Applicants maintain the arguments presented in the two Replies filed August 26, 2002 and November 26, 2002

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the reference and the reference must teach or suggest all of the claim limitations. The Examiner has not provided any motivation to modify Altmann et al. Further, Altmann et al. do not teach or suggest all of the limitations of Applicants' claim. As stated in M.P.E.P. 2143.03, "To establish prima facie obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art." In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

The Examiner alleges that "Altmann et al. teaches R_3 (corresponding to instant R_2) as "cyclo-lower hydrocarbyl"(which is defined on page 2, first line of second paragraph); the prior art R_2 corresponds to hydrogen of the instant claim; the group $-NH_2$ (corresponding to instant $N(R_3)_2$ and the overlap at both the instant and prior art R_1 is seen in the definition of R_1 on pages 1-4 of the reference". However, an invention is to be considered as a whole. That is, in this case, does Atlmann et al. make obvious the entire genus of any of Applicants' claims? The claimed invention may not be dissected into discrete elements to be analyzed in isolation, but must be considered as a whole. See, e.g. W.L. Gore & Assoc. Inc. v. Garlock, Inc. 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983)); Jones v. Hardy, 727 f.2d 1524, 1530, 220 USPQ 1021, 1026 (Fed. Cir. 1983). In determining the differences between the prior art and the claims, the question under 35 U.S.C. §103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); Schenck v. Nortron Corp.,713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). The Examiner has not shown how Altmann et al. renders obvious the entire genus of Applicants' claim. Applicants maintain that Altmann et al.does not render claims 1-88 obvious.

The Examiner alleges that the reference teaches a generic group of substituted 7-amino-pyrrolo[3,2-d]pyrimidine derivatives which embraces Applicants' claimed compounds. Simply because a very few of Applicants' examples are encompassed by the broad genus of Altmann et al does not establish a *prima facie* case of obviousness. The fact that a claimed species or

subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness as to the entire genus of Claim 1. Additionally, none of the dependent compound claims 2-32 or 52-88 fall within Altmann et al. because in Applicants' R_1 and R_2 are much more expansive than Altmann et al.'s corresponding R_1 and R_3. In addition, Applicants' R_a includes additional substituents not disclosed in Altmann et al. and, thus, is not fully encompassed by Altmann et al. Further, in Applicants' dependent claims where Applicants' R_3 is hydrogen and thus overlaps with Altmann et al in that position, Applicants' R_2 and R_3 do not overlap with the corresponding positions in Altmann et al. In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious"); In re Jones, 958 F2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992). The fact that there is a slight overlap with Altmann et al. does not make Applicants' entire genus obvious. The Examiner has not met his burden for a *prima facie* obviousness rejection.

Based upon the foregoing, the rejection of claim 1-88 under 35 U.S.C. §103(a) over Altmann et al. (WO 97/49706) is obviated and should be withdrawn.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 1-40 and 44-88 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Respectfully submitted,

Date: July 28, 2003

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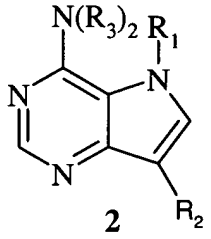
APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

1. (Currently Amended) A compound of Formula (I), the racemic-diastereomeric mixtures, optical isomers or pharmaceutically-acceptable salts [or prodrugs] thereof,



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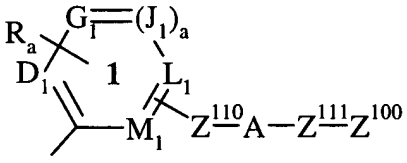
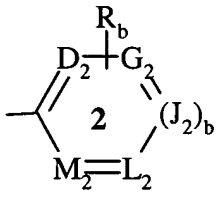
wherein:

R_1 is 

1

where Z^{100} is 

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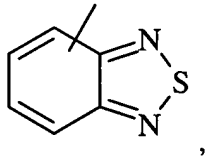
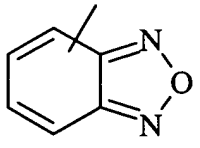
or a group optionally substituted with R_b selected from the group consisting of cycloalkyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl, thienyl, benzoxazolyl, benzothiazolyl,  ,  , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, benzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN,

OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted -$(CH_2)_n$-cycloalkyl-$(CH_2)_n$-; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_1 each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, -NO_2, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z^{105}-C(O)N$(R)_2$, -Z^{105}-N(R)-C(O)-Z^{200}, -Z^{105}-N(R)-S$(O)_2$-Z^{200}, -Z^{105}-N(R)-C(O)-N(R)-Z^{200}, R_c and CH_2OR_c;

where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, -CH_2-NR_dR_e, -W-$(CH_2)_t$-NR_dR_e, -W-$(CH_2)_t$-Oalkyl, -W-$(CH_2)_t$-S-alkyl, or -W-$(CH_2)_t$-OH;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6);

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6), substituted or unsubstituted phenyl or substituted or unsubstituted -(C_1-C_6)-phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2-alkyl; or R_d, R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring; t for each occurrence is independently an integer from 2 to 6; W for each occurrence is independently a direct bond or O, S, S(O), $S(O)_2$, or NR_f, wherein R_f for each occurrence is independently H or alkyl;

or R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 is hydrogen, hydroxy, substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy;

A is -O-; -S-; -$S(O)_p$-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -$N(SO_2R)$-; -CH_2O-; -CH_2S-; -$CH_2N(R)$-; -CH(NR)-; -$CH_2N(C(O)R)$)-; -$CH_2N(C(O)OR)$-; -$CH_2N(SO_2R)$-; -CH(NHR)-; -CH(NHC(O)R)-; -$CH(NHSO_2R)$-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR); -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; -$N(R)S(O)_p$-; -OC(O)N(R)-; ; -N(R)-C(O)-$(CH_2)_n$-N(R)-, -N(R)C(O)O-; -N(R)-$(CH_2)_{n+1}$-C(O)-, -$S(O)_pN(R)$-; -O-$(CR_2)_{n+1}$-C(O)-, -O-$(CR_2)_{n+1}$-O-, -$N(C(O)R)S(O)_p$-; -$N(R)S(O)_pN(R)$-; -N(R)-C(O)-$(CH_2)_n$-O-, -C(O)N(R)C(O)-; -$S(O)_pN(R)C(O)$-; -$OS(O)_pN(R)$-; -$N(R)S(O)_pO$-; -$N(R)S(O)_pC(O)$-; -$SO_pN(C(O)R)$-; -$N(R)SO_pN(R)$-; -C(O)O-; -$N(R)P(OR_g)O$-; -$N(R)P(OR_g)$-; -$N(R)P(O)(OR_g)O$-; -$N(R)P(O)(OR_g)$-; -$N(C(O)R)P(OR_g)O$-; -$N(C(O)R)P(OR_g)$-; -$N(C(O)R)P(O)(OR_g)O$-, or -$N(C(O)R)P(OR_g)$-;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_g for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2;

or in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_g together form a five- or six-membered heterocyclic ring; or

A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or-six-membered heterocyclic ring fused to ring 1;

R_2 is -Z^{101}-Z^{102};

Z^{101} is a covalent bond, -(C_1-C_6)-, -(C_1-C_6)-O-, -(C_1-C_6)-C(O)-, -(C_1-C_6)-C(O)O-, -(C_1-C_6)-C(O)-NH-, -(C_1-C_6)-C(O)-N((C_1-C_6))- or a substituted or unsubstituted phenyl group;

Z^{102} is hydrogen, a substituted or unsubstituted alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted, saturated or unsaturated heterocyclic group, or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group;

said substituted heterocyclic or substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, substituted or unsubstituted alkoxy, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido; substituted or unsubstituted amino, oxo, a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more nitrogen atoms, one or more oxygen atoms or a combination thereof;

wherein said nitrogen atoms are independently optionally substituted by a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; or

R_2 is of the formula B-E, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalklylcarbonyl, hydroxy, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylenecarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted azacycloalkyl, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino or substituted or unsubstituted aryl;

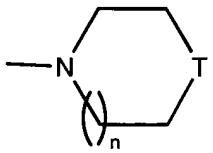
a is 1 and D_1, G_1, J_1, L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1, G_1, J_1, L_1 and M_1 are CR_a; or

a is 0, and one of D_1, G_1, L_1 and M_1 is NR_a, one of D_1, G_1, L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

b is 1 and D_2, G_2, J_2, L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2, G_2, J_2, L_2 and M_2 are CR_a; or

b is 0, and one of D_2, G_2, L_2 and M_2 is NR_a, one of D_2, G_2, L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6.



wherein

T is C(O), S, SO, SO_2, CHOR or NR, wherein R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; and

n is 0, 1 or 2.

34. (Amended) A method of inhibiting one or more protein kinase activity in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt [or prodrug] thereof to said patient.

35. (Amended) A method of affecting [hyperproliferative disorders] <u>thyroid hyperplasia, Grave's disease, cyst, hypervascularity of ovarian stroma characteristic of polycystic ovarian syndrome and polycystic kidney disease</u> in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt [or prodrug] thereof to said patient.

36. (Amended) A method of affecting angiogenesis in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt [or prodrug] thereof to said patient.

38. (Amended) A method of treating one or more ulcers in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt [or prodrug] thereof to said patient.

40. (Amended) A method of treating a condition in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt [or prodrug] thereof to said patient, wherein said condition is an ocular condition, [a cardiovascular condition, a cancer,] Crow-Fukase (POEMS) syndrome, a diabetic condition, sickle cell anaemia, chronic inflammation, systemic lupus, glomerulonephritis, synovitis, inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, graft rejection, Lyme disease, sepsis, von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease, polycystic kidney disease, fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease, asthma or edema following burns, trauma, radiation, stroke, hypoxia, ischemia, ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, endometriosis, or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa,[or] toxoplasmosis, a solid tumor, a sarcoma, fibrosarcoma, osteoma, melanoma, retinoblastoma, a rhabdomyosarcoma, glioblastoma, neuroblastoma, teratocarcinoma, an hematopoietic malignancy, Kaposi's sarcoma, Hodgkin's disease, lymphoma, myeloma, leukaemia, malignant ascites, atherosclerosis, restenosis, ischemia/reperfusion injury, vascular occlusion, carotid obstructive disease, ocular or macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser treatment complications, conjunctivitis, Stargardt's disease, Eales disease, retinopathy or macular degeneration.

45. (Amended) A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Claim 1 or a physiologically acceptable salt [or prodrug] thereof.

46. (Twice Amended) The method of Claim 36 wherein the compound or a physiologically acceptable salt [or prodrug] thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.

48. (Twice Amended) The method of Claim 46 wherein the compound of Formula I, or physiologically acceptable salt [or prodrug] thereof, is administered in combination with a pro-angiogenic growth factor.